27. (New) A test kit useful for detecting a target polynucleotide indicative of gastro-intestinal GI tract tissue disease in a test sample, said test kit comprising a container containing at least one reagent polynucleotide comprising at least about 10 nucleotides that (i) specifically binds, and (ii) has at least 90% identity with a polynucleotide selected from the group consisting of consisting of SEQUENCE ID NO 1; SEQUENCE ID NO 2; SEQUENCE ID NO 4; SEQUENCE ID NO 5; SEQUENCE ID NO 23; SEQUENCE ID NO 24; SEQUENCE ID NO 25; and complements thereof.

II. REMARKS

Claims 1-18 are pending. Claims 7-10, 13, 14 and 16 have been withdrawn pursuant to a restriction requirement. Claims 1-6, 11, 12, 15, 17 and 18 stand various rejected under §§ 112, first and second paragraphs, 102 and 103.

By amendment herein claim 1 has been amended; claims 4, 5, 6, 11, 12, 15, 17 and 18, without prejudice or disclaimer; and new claims 19-27 have been added. Cancellation or amendment of claims 4, 5, 6, 11, 12, 15, 17 and 18 is not intended to be an acquiescence in the Office's assessment of those claims, and Applicants expressly reserve the right to bring the subject matter of the original claims again in a subsequent, related application.

Basis for the amendments and newly added claims can be found as follows. Support for the amendment to claim 1 can be found, for example, on page 1, lines 5-8 which incorporate by reference the disclosure of U.S. Serial No. 08/828,845. This application included the sequences now identified as SEQ ID NO: 23 (clone 1430502), SEQ ID NO: 24 (clone 2513529) and SEQ ID NO: 25 (clone 958984). The specification (Example 1, page 52) has been amended to incorporate this information.

Basis for new claims 19-27 can be found throughout the specification, for example, at page 11, line 12 and page 18, lines 17-21 ("indicative of a GI tract tissue disease or condition"); pages 5-9 ("target polynucleotide"); page 12, lines 17-21 ("10 nucleotides"); page 17, lines 8-20 ("test sample"); page 24, lines 12-15; page 25, lines 20-26 and page 26, line 27 to page 27, line 6 ("detecting mRNA" and "reverse

transcriptase"); page 26, line 32, page 19, line 32 to page 20, line 3, and page 24, lines 12-14 ("detectable label"); and page 50, line 9 ("test kit"). Basis for the recitation of "specifically binds" and "at least 90% identity" is discussed in detail below.

Thus, no new matter has been added by way of this amendment and the entry thereof is respectfully requested.

Oath/Declaration

The oath and declaration is alleged to be defective for failing to claim priority as states in the first paragraph of the pending specification. Applicants are currently executing a new oath and declaration and will forward it as soon as possible.

Sequence Listing

Attached hereto is an updated Sequence Listing. This Sequence Listing includes SEQ ID NO:23, SEQ ID NO:24 and SEQ ID NO:25 (incorporated by reference from U.S. Serial No. 08/828,845). Support for addition of these sequences is described above.

Rejection of Claims 17 and 18 under 35 U.S.C. §101

The Examiner has rejected claims 17 and 18 under 35 U.S.C. §101 asserting that the claims are directed to non-statutory subject matter. Claims 17 and 18 have been canceled by amendment herein, thereby obviating this rejection. In addition, the claims as amended are all directed to "purified polynucleotides" and, therefore, are directed to statutory subject matter.

Rejection of Claims 1-6, 12, 15, 17-18 under 35 U.S.C. §112, Second Paragraph

The Examiner has rejected claims 1-6, 12, 15, 17-18 under 35 U.S.C. § 112, second paragraph, asserting that the claims are indefinite for failing to particularly point out and distinctly claim the subject matter which the applicant regards as the invention. The Examiner has asserted the following specific deficiencies in the claims.

Although the claims 3-6, 12, 15, 17-18 have been canceled and claims 1, 2 and 3 amended to obviate this rejection, new claims 19-27 include similar language. Accordingly, Applicants address the recited terms below.

A. "Percent identity"

The Examiner asserts that recitation of "% identity" is vague and indefinite. Applicants disagree with the Examiner's assessment of the level of enabling disclosure in the present applicant in regard to "percent identity." The applicants discuss the use of available programs for calculating identity or similarity between sequences in the specification (e.g., page 10, line 28 to page 11, line 10). Applicants submit that use of default parameters in such programs is routine and well within the abilities of one having ordinary skill in the art -- this is the manner in which the Examiner has searched the database for sequences that may correspond to the claimed sequences. Further, at the AIPLA meeting in Crystal City, Fall of 1999, Examiner John Doll stated that the USPTO policy toward claims reciting percent identity has changed and that Examiners will no longer be rejecting percent identity claims under 35 U.S.C. §112, second paragraph.

B. "Selectively hybridization"

Applicants traverse this rejection.

It is well-settled that absolute specificity and precision are not required in the claims. Claims need only reasonably apprize a person having ordinary skill in the art as to their scope. *Hybritech Inc., v. Monoclonal Antibodies, Inc.*, 231 USPQ 81, Fed. Cir. 1986. The second paragraph of 35 U.S.C. §112 merely requires that an applicant set out and circumscribe a particular subject area with a reasonable degree of precision such that the metes and bounds of the invention are set forth. *Ex parte Head*, 214 USPQ 551, PTO Bd. App. 1981.

However, in an effort to facilitate prosecution, Applicants have deleted the language "hybridization" from the pending claims, as suggested by the Examiner. Applicants have introduced the language "a polynucleotide that specifically binds to a

polynucleotide sequence." The specification provides extensive basis for use of this language. For example, on page 20, lines 1-12, detection of an analyte is discussed wherein a specific binding member is prepared for binding to a target analyte such as a nucleotide target. On page 18, line 31 through page 19, line 6, a definition of "specific binding members" is discussed, wherein a "specific binding member" is a member of a specific binding pair (see also, e.g., page 20, lines 4-29; page 19, lines 10-31; and page 7, line 22, to page 8, line 36). That is, two different molecules where one of the molecules, through chemical or physical means, specifically binds to the second molecule. Specific binding pairs can include complementary nucleotide sequences. On pages 21-24, the specification describes how the sequences provided in the application may be used to produce polynucleotide sequences (for example, primers and probes; also see, e.g., page 12, lines 22-29 for definitions of primers and probes; page 24, lines 18-27 for a description of probe assays) which can be used in assays for the detection of target nucleic acids in test samples, via specifically binding the polynucleotide sequences to the target. Probes may, for example, be designed from conserved nucleotide regions of the polynucleotides of interest or from non-conserved nucleotide regions of the polynucleotide of interest. The design of such probes for optimization in assays is within the skill of the routineer. Generally, nucleic acid probes are developed from non-conserved or unique regions when maximum specificity is desired, and nucleic acid probes are developed from conserved regions when assaying for nucleotide regions that are closely related to, for example, different members of a multi-gene family or in related species like mouse and man. Numerous examples are given in the specification that would allow one of ordinary skill in the art to determine the metes and bounds of the invention (e.g., Examples 1-11, pages 51-70). For example, selection of primers for use in polymerase chain reactions is described at least on page 24, lines 28-36 and exemplary conditions (including hybridization conditions) for such reactions are described in the Examples (e.g., Examples 3, 4, 8 and 9).

Use of probes in fluorescent in situ hybridization (FISH) technology to perform chromosomal analysis is also described herein. Such an approach can be used to identify

cancer-specific structural alterations in the chromosomes, such as deletions or translocations that are visible from chromosome spreads or detectable using PCR-generated and/or allele specific oligonucleotides probes, allele specific amplification or by direct sequencing. Probes also can be labeled with radioisotopes, directly- or indirectly- detectable haptens, or fluorescent molecules, and utilized for *in situ* hybridization studies to evaluate the mRNA expression of the gene comprising the polynucleotide in tissue specimens or cells (page 24, lines 5-15; and Example 7, pages 59-60). Use of the polynucleotide sequences of the present invention in such technology is another example of specific binding of a polynucleotide sequence to a target.

The characteristics and properties of polynucleotides of the present invention for use in hybridization reactions (including probes and amplification primers) are extensively discussed in the specification in the context of specific binding (see, for example, pages 24-31). Further, examples using polynucleotides in hybridization reactions are discussed in the application, including suitable reaction conditions (e.g., Examples 5, 6, and 7, pages 58-60).

The court has consistently stated that claim language must be read in light of prior art and teachings of the specification. The standard is that the "definiteness of the language must be analyzed...in light of the teachings of the prior art and of the particular application disclosure as it would be interpreted by one possessing the ordinary level of skill in the pertinent art." *In re Moore*, 439 F.2d 1232, 169 USPQ 236 (CCPA 1971). A claim which is clear to one ordinarily skilled in the art when read in light of the specification, does not fail for indefiniteness. *Slimfold Mfg. Co. v. Kinkead Indus., Inc.*, 932 F2d 1453, 1 USPQ2d 1536 (Fed. Cir 1986).

In view of the above amendments, the teachings of the specification and the level of ordinary skill in the present art, the applicants submit that the boundaries of the claims are capable of being understood by one of ordinary skill in the art. Therefore, withdrawal of the rejection of the claims under 35 U.S.C. §112, second paragraph, is respectfully requested.

No new matter has been entered by way of these amendments. Accordingly, entry of the amendments is respectfully requested. In view of the above amendments and comments the Applicants submit that claims !comply with the requirements of 35 U.S.C. §112, second paragraph, and the rejection of the claims should be withdrawn.

Rejection of Claims 1-4, 17 and 18 under 35 U.S.C. §112, First Paragraph

The Examiner has rejected claims 1-4, 17 and 18 under 35 U.S.C. § 112, first paragraph, asserting that the claims allegedly contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. In particular, the specification is alleged not to provide a written description of claims drawn to a "gene."

Without conceding the correctness of the Examiner's position and solely to advance prosecution, claim 1 has been amended herein such that the term "gene" is no longer contained therein. Claims 17 and 18 have been canceled. The newly added claims also do not recite this term. Accordingly, this rejection has been obviated and Applicants respectfully request that it be withdrawn.

Rejection of Claims 1, 2, 4-6, 11, 15 and 18 Under 35 U.S.C. §102(b)

The Examiner has rejected claims 1, 2, 4-6, 11, 15 and 18 under 35 U.S.C. §102(b) asserting that the claim is anticipated by Adams et al. (Genebank accession number AA2999777; Nature, vol 377, Supp., page 3-16, 28, Sept. 1995). In particular, The Examiner asserts that Adams, et al., teach a fragment having 93% identity to SEQ ID NO:1, 96% identity to SEQ ID NO:2 and a fragment from positions 192-243 identical to SEQ ID NO:1 from positions 203-254 and a fragment from positions 192-258 identical to SEQ ID NO: 2 from positions 195-261. (Office action, page 7, first paragraph).

For prior art to anticipate under 35 U.S.C. 102 it has to meet every element of the claimed invention: such a determination is one of fact. *Hybritech Inc. v. Monoclonal Antibodies*, 802 F.2d at 1367, 231 USPQ 81 (Fed. Cir. 1986).

As amended herein, claim 1 is drawn to the specific sequences of SEQ ID Nos: 1, 2, 23, 24, 25 and complements thereof. The prior art sequence (AA299977) cited by the Examiner does not teach these precisely claimed sequences. Further, with respect to the newly added method claims, there is simply no teaching in the reference that the sequence would be useful in detecting GI tract tissue diseases. Thus, the prior art cited by the Examiner fails to teach at least the following limitations of the pending independent claims:

(a) independent claim 1 (as amended): a polynucleotide consisting of a polynucleotide selected from the group consisting of SEQ ID Nos: 1, 2, 23, 24, 25 and complements thereof;

(b) independent claims 19, 21, 24 and 27 (newly added): methods of detecting a GI tract tissue disease or disorder using the claimed sequences, fragments and complements thereof.

In view of the above amendments and arguments, the cited reference sequence cannot be said to teach all the elements of the present invention. The dependent claims distinguish over the prior art at least in view of their dependencies on the independent claims. Accordingly, there is no support for the pending claims being anticipated by the cited prior art under 35 U.S.C. §102(b) and withdrawal of the rejection is respectfully requested.

Rejection of Claims 12 and 17 Under 35 U.S.C. §102(e)

The Examiner has rejected claims 12 and 17 under 35 U.S.C. §102(e) asserting that the claim is anticipated by Lal et al. (U.S. Patent No. 5,856,139, Jan 5, 1999).

By amendment herein, Applicants have canceled claims 12 and 17, thereby obviating this rejection. Therefore, withdrawal of this rejection is respectfully requested.

Rejections of the Claims 1, 3, 5, 6 and 11 Under 35 U.S.C. §103

The Examiner has rejected claims 1, 3, 5, 6 and 11, under 35 U.S.C. §103(a) as being unpatentable over Adams et al. or Hillier et al. (Genbank EST, Accession No. T78178, submitted on March 15, 1995; and Accession NO. T85589, submitted on March

17, 1995) in view of Olson et al. (U.S. Patent No. 4,889,806) and Sambrook et al. (Molecular Cloning, a Laboratory Manual, 1989, Cold Spring Harbor Press, p. 16.3-4).

Applicants traverse this rejection.

It is axiomatic that Obviousness cannot be established by combining teachings in the prior art absent some teaching or suggestion in the prior art that the combination be made. E.g., *In re Stence,* 828 F. 2d 751, 4 USPQ2d 1071 (Fed. Cir. 1987); *In re Newell*, 891 F. 2d 899, 13 USPQ2d 1248 (Fed Cir 1989). In particular, the fact that references can be combined does not make the combination obvious unless the prior art also contains something to suggest the desirability of that combination. *In re Sernaker*, 702 F.2d 989, 217 USPQ 1 (Fed,. Cir. 1983). The PTO has the burden of establishing a case of *prima facie* obviousness, and can meet this burden "only by showing some objective teaching in the prior art or that knowledge generally available to one of ordinary skill in the art would lead that individual to combine the relevant teachings of the references." *In re Fine*, 837 F.2d 1071, 5 USPQd2 1596 (Fed. Cir. 1988). No such objective teaching has been presented.

With regard to claim 1, as noted above, there is no teaching or suggestion within the references to arrive at the precisely claimed polynucleotides. None of the primary references (Adams and Hillier) disclose the precise sequences recited in claim 1. Thus, combining these distinguishable sequences with references teaching general methods of molecular biology (Olson and Sambrook) does not establish a *prima facie* case of obviousness. Moreover, there is no guidance concerning the selection of the three cited sequences from among the millions of possible sequences available in the database (i.e., GENBANK or EMBL). Thus, the combination of references cited does not render claim 1, as amended, unpatentable.

Further, the newly added independent claims 19, 21, 24 and 27 each recite a limitation similar to the following: "a method of detecting the presence of a target polynucleotide indicative of GI tract tissue disease." None of the references singly or in combination teach that detection of the polynucleotides of the present invention may be indicative of GI tract tissue disease.

Accordingly, because the elements of the claimed invention are not taught by the cited references, the applicants submit that the rejections under 35 U.S.C. §103 should be withdrawn.

III. CONCLUSION

Applicants respectfully submit that the claims comply with the requirements of 35 U.S.C. §112 and define an invention that is patentable over the art. Accordingly, a Notice of Allowance is believed in order and is respectfully requested.

If the Examiner notes any further matters which the Examiner believes may be expedited by a telephone interview, the Examiner is requested to contact the undersigned.

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